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     (FILE 'HOME' ENTERED AT 13:11:26 ON 05 SEP 2007)

     FILE 'CAPLUS, MEDLINE' ENTERED AT 13:11:56 ON 05 SEP 2007
L1             0 S HYALURONIC ACID (P) ANAESTATHETIC?
L2             6 S HYALURONIC ACID (P) ANAESTHETIC?
L3             3 S HYALURONATE (P) ANAESTHETIC?
L4             6 S HYALURONIC ACID? (P) ANAESTHETIC?
L5             3 S HYALURONATE? (P) ANAESTHETIC?
L6             2 S HYALURONAN? (P) ANAESTHETIC?
L7             2 S HYALURONIC ACID? (P) ARTICULAR (P) ADDITIVES?
L8            11 S HYALURONIC ACID? (P) ARTICULAR (P) ADJUVANT?
L9           823 S HYALURONIC ACID? (P) ARTICULAR?
L10            3 S HYALURONIC ACID? (P) ARTICULAR? (P) ASCORB?
L11            0 S HYALURONIC ACID? (P) ARTICULAR? (P) TOCOPHEROL?
L12            0 S HYALURONIC ACID? (P) TOCOPHEROL? (P) CONJUNTI?
L13            8 S HYALURONIC ACID? (P) TOCOPHEROL? (P) ASCORB?
L14            4 S HYALURONIC ACID? (P) TOCOPHEROL? (P) INHIBITOR?
L15            1 S HYALURONIC ACID? (P) TOCOPHEROL? (P) GROWTH FACTOR?
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     (FILE 'HOME' ENTERED AT 13:11:26 ON 05 SEP 2007)

     FILE 'CAPLUS, MEDLINE' ENTERED AT 13:11:56 ON 05 SEP 2007
L1             0 S HYALURONIC ACID (P) ANAESTATHETIC?
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L8            11 S HYALURONIC ACID? (P) ARTICULAR (P) ADJUVANT?
L9           823 S HYALURONIC ACID? (P) ARTICULAR?
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L11            0 S HYALURONIC ACID? (P) ARTICULAR? (P) TOCOPHEROL?
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L13            8 S HYALURONIC ACID? (P) TOCOPHEROL? (P) ASCORB?
L14            4 S HYALURONIC ACID? (P) TOCOPHEROL? (P) INHIBITOR?
L15            1 S HYALURONIC ACID? (P) TOCOPHEROL? (P) GROWTH FACTOR?
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L2 ANSWER 1 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2004622055 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15518947
TITLE: [Soft tissue filling with hyaluronic acid].
Les comblements par l'acide hyaluronique.
AUTHOR: Ascher B; Cerceau M; Baspeyras M; Rossi B
CORPORATE SOURCE: Clinique IENA, 11, rue Fresnel, 75116 Paris, France..
benjaminascher@wanadoo.fr
SOURCE: Annales de chirurgie plastique et esthetique, (2004 Oct)
Vol. 49, No. 5, pp. 465-85. Ref: 64
Journal code: 8305839. ISSN: 0294-1260.
PUB. COUNTRY: France
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20 Dec 2004
Last Updated on STN: 25 Jan 2005
Entered Medline: 24 Jan 2005

AB PHYSIOLOGY AND PHARMACOLOGY: Hyaluronan was discovered by Karl Meyer in 1934 in the vitreous humor of cattle eye. Hyaluronic acid, (AH), is a natural polysaccharide and a ubiquitous component of the extra cellular matrix. It is largely biocompatible and has a short half life. In the early 1990's, preceded by the use of bovine collagen, AH started to be employed in the fields of Dermatology and Plastic Surgery; currently it is a major intervention product in both soft tissue augmentation and facial volume loss treatments. Often well tolerated, AH, has high water retention properties and is an effective tissue volumizer. Industry first attempted to extract AH from rooster comb, then through bacterial fermentation and succeeded in increasing its lifespan by cross linking. However, industrially produced AH can contain residues from the manufacturing process. It thus appears critical to us to be informed of the process used in manufacturing AH including the reticulant utilized. Manufacturers should be legally required to publish this data as well as to conduct physiochemical follow-up studies over the short, mid and long terms. LEGAL CONSIDERATIONS: In Europe, CE marking is a prerequisite to market injectable products. However, a CE marking does not necessarily imply that the product's efficacy and side effects have been assessed objectively in clinical studies. However, this marking is expected to fall into line with the US legislation, where the marketing of any medicinal product is subject to FDA approval, based on comprehensive animal and clinical studies and on more systematic and better centralised side effect reporting. We have examined most of the products used in Europe and internationally in 2004, whether of animal or bacterial origin, reticulated or non-reticulated, and used to restore, increase volume or as a product vector. Before injecting these products, it is essential to have a thorough understanding of their absolute and relative contraindications and anaesthetic requirements, differences between types of wrinkles to fill in and indicated techniques, differences between concerned regions or tissues, and the impact of associated cosmetic treatments. These resorbable injectable products have mild and, more importantly, short-lived side effects. However, in patients with a relative contraindication, a double test is justified, as allergic reactions are known to occur in 1 to 3% of patients. It is also advisable not to inject HA in a site previously injected with a non-resorbable product. More precise statistics on results and side effects based on double-blind randomised studies are still wanting, due to the lack of legal requirement and effective centralisation of data. Therefore, all side effects must be reported to improve our knowledge as well as the safety of injections. CONCLUSION: Although their duration of effect is limited, HA products are the most commonly used fillers, before collagens.

Many questions have yet to be answered, but they produce very significant results in filling procedures. Both clinicians and patients praise these products for their tolerance, resorbable nature, and limited side effects.

L2 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2004301919 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15206412
TITLE: Tetrodotoxin-induced conduction blockade is prolonged by hyaluronic acid with and without bupivacaine.
AUTHOR: Stevens M F; Hoppe M; Holthusen H; Lipfert P
SOURCE: Acta anaesthesiologica Scandinavica, (2004 Mar) Vol. 48, No. 3, pp. 128-34.
Journal code: 0370270. ISSN: 0001-5172.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: (CORRECTED AND REPUBLISHED ARTICLE)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 24 Jun 2004
Last Updated on STN: 24 Jun 2004
Entered Medline: 21 Jun 2004

AB BACKGROUND: In isolated nerves, tetrodotoxin (TTX) blocks nerve conduction longer than bupivacaine. In vivo, however, both substances block nerve conduction to an equal duration, presumably because the hydrophilic TTX binds only weakly to the perineural tissue. High molecular weight hyaluronic acid (HA) prolongs the action of local anaesthetics several-fold. We tested whether admixture of HA enhances the binding of TTX to the perineural tissue and thus induces an ultra-long conduction block after a single application. METHODS: In 12 anaesthetized rabbits, the minimal blocking concentrations of TTX, TTX and HA (TTX/HA) and bupivacaine with HA (bupivacaine/HA) were determined by blocking the natural spike activity of the aortic nerve. In 18 other animals, equipotent concentrations of either TTX, TTX/HA or TTX/bupivacaine/HA were applied topically to the aortic nerve. After disappearance of the spike activity, the wound was closed to simulate the clinical situation of a single shot nerve block. The time until recovery of spike activity was determined. The nerves were examined for signs of neurotoxicity 24 h after the application of the drugs. Data are presented as means +/- SD and compared by ANOVA and Student's t-test for unpaired data. RESULTS: The conduction block by TTX/bupivacaine/HA (10.1 +/- 1.9 h) or TTX/HA (9.3 +/- 1.0 h) was significantly longer than that of plain TTX (7.9 +/- 1.0 h). Neurotoxicity was not observed. CONCLUSIONS: Both HA and HA/bupivacaine prolong the TTX-induced conduction blockade of the aortic nerve of rabbits in vivo. No signs of neurotoxicity were observed.

L2 ANSWER 3 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2003593553 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14674985
TITLE: Tetrodotoxin-induced conduction blockade is prolonged by hyaluronic acid with and without bupivacaine.
AUTHOR: Stevens M F; Hoppe M; Holthusen H; Lipfert P
CORPORATE SOURCE: Klinik fur Anaesthesiologie, Universitatsklinikum Dusseldorf, Postfach 101007, 40001 Germany.. markus.stevens@med.uni-duesseldorf.de
SOURCE: Acta anaesthesiologica Scandinavica, (2004 Jan) Vol. 48, No. 1, pp. 128-34.
Journal code: 0370270. ISSN: 0001-5172.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 17 Dec 2003

Last Updated on STN: 20 Apr 2004
Entered Medline: 19 Apr 2004

AB BACKGROUND: In isolated nerves, tetrodotoxin (TTX) blocks nerve conduction longer than bupivacaine. In vivo, however, both substances block nerve conduction to an equal duration, presumably because the hydrophilic TTX binds only weakly to the perineural tissue. High molecular weight hyaluronic acid (HA) prolongs the action of local anaesthetics several-fold. We tested whether admixture of HA enhances the binding of TTX to the perineural tissue and thus induces an ultra-long conduction block after a single application. METHODS: In 12 anaesthetized rabbits, the minimal blocking concentrations of TTX, TTX and HA (TTX/HA) and bupivacaine with HA (bupivacaine/HA) were determined by blocking the natural spike activity of the aortic nerve. In 18 other animals, equipotent concentrations of either TTX, TTX/HA or TTX/bupivacaine/HA were applied topically to the aortic nerve. After disappearance of the spike activity, the wound was closed to simulate the clinical situation of a single shot nerve block. The time until recovery of spike activity was determined. The nerves were examined for signs of neurotoxicity 24 h after the application of the drugs. Data are presented as means +/- SD and compared by ANOVA and Student's t-test for unpaired data. RESULTS: The conduction block by TTX/bupivacaine/HA (10.1 +/- 1.9 h) or TTX/HA (9.3 +/- 1.0 h) was significantly longer than that of plain TTX (7.9 +/- 1.0 h). Neurotoxicity was not observed. CONCLUSIONS: Both HA and HA/bupivacaine prolong the TTX-induced conduction blockade of the aortic nerve of rabbits in vivo. No signs of neurotoxicity were observed.

L2 ANSWER 4 OF 6 MEDLINE on STN
ACCESSION NUMBER: 93092889 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1459055
TITLE: Septic arthritis in 15 standardbred racehorses after intra-articular injection.
AUTHOR: Lapointe J M; Laverty S; Lavoie J P
CORPORATE SOURCE: Departement de Medecine, Faculte de Medecine Veterinaire, Universite de Montreal, Saint-Hyacinthe, Quebec, Canada.
SOURCE: Equine veterinary journal, (1992 Nov) Vol. 24, No. 6, pp. 430-4.
Journal code: 0173320. ISSN: 0425-1644.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 29 Jan 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 8 Jan 1993

AB Case histories, results of synovial fluid analyses, treatment regimens and outcome are described for 15 adult Standardbred horses with confirmed post-injection septic arthritis. Joint sepsis followed injection of corticosteroids, hyaluronic acid, polysulphated glycosaminoglycan, or local anaesthetic. The median interval from injection to appearance of clinical signs was 2.5 days, and median interval from injection to referral was 9 days. The median initial synovial leucocyte count on admission was 57 x 10(9)/litre, but there was a wide range of values (18-258 x 10(9)/litre). The median synovial neutrophil percentage was 95% (77-99%). All bacterial isolates were Gram-positive cocci, 86% of which were staphylococci. All treated horses (12/15) initially received broad-spectrum parenteral antibiotic therapy, and the articulations of all horses except one were lavaged, either with non-surgical through-and-through techniques only (N = 3), or surgically with arthrotomy (N = 1) or arthroscopy (N = 7). The owners of all treated horses were contacted and racing records were consulted. Eleven of 12 horses returned to racing. Outcome was judged as either satisfactory (3/12) if the horse had returned to racing levels similar to or better than before treatment, or unsatisfactory (9/12) if the horse had poorer

performance or could not return to racing. The 3 horses with satisfactory follow-up had been treated with arthroscopy and post-surgical closed suction drainage. The results of bacterial cultures suggest that the initial antimicrobial agents used should be effective against penicillin-resistant staphylococci.

L2 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 86073261 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4072599
TITLE: Effects of adjuvants to local anaesthetics on their duration. IV. Effect of hyaluronic acid added to bupivacaine or prilocaine on the duration of nerve blockade in man.
AUTHOR: Johansson A; Hassan H; Renck H
SOURCE: Acta anaesthesiologica Scandinavica, (1985 Oct) Vol. 29, No. 7, pp. 736-8.
Journal code: 0370270. ISSN: 0001-5172.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198601
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 29 Jan 1999
Entered Medline: 17 Jan 1986
AB A randomized study of the duration of ulnar nerve blockade induced with 2% prilocaine or 0.5% bupivacaine with and without 0.4% hyaluronic acid was performed in volunteers. In contrast to results in experimental animals, the addition of hyaluronic acid to the local anaesthetic solution did not affect the duration of sensory nerve block.

L2 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 85247331 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3874511
TITLE: Effects of adjuvants to local anaesthetics on their duration. III. Experimental studies of hyaluronic acid.
AUTHOR: Hassan H G; Akerman B; Renck H; Lindberg B; Lindquist B
SOURCE: Acta anaesthesiologica Scandinavica, (1985 May) Vol. 29, No. 4, pp. 384-8.
Journal code: 0370270. ISSN: 0001-5172.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198508
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 21 Aug 1985
AB The effects of addition of hyaluronic acid (sodium hyaluronate, Healon) to different local anaesthetics of the amide type on the duration of sensory or motor blocks following various regional anaesthetic procedures were studied in animal experiments. In the rat infra-orbital nerve block model, the addition of 0.1-0.5% hyaluronic acid (HA) to 2% prilocaine increased the duration of sensory block of varying degrees in a dose-dependent way by up to 500% of values obtained with plain prilocaine. The duration of degree 5 blocks produced by 0.5% etidocaine and 0.5% bupivacaine was also significantly prolonged when 0.4% HA was included to 206% and 282% of control, respectively, while blocks induced by 2% lidocaine were prolonged to 123% of control. The duration of motor block following spinal anaesthesia in the mouse was prolonged in a

dose-dependent way when HA was added to prilocaine, bupivacaine and etidocaine. For solutions containing 0.4% HA, prolongations to 254%, 166% and 134% of control, respectively, were obtained. A concomitant increase of latency to onset of block and failure rate occurred with increasing concentrations of HA. The duration of corneal anaesthesia in the rabbit increased by 57% and 44% when 0.3% HA was added to prilocaine and bupivacaine, respectively. The duration of infiltration anaesthesia was not affected by the addition of HA to the local anaesthetic solutions. Addition of HA had no effect on the onset, depth and duration of prilocaine-induced block of the nervous transmission in vitro. The duration of infra-orbital nerve block and spinal anaesthesia shows a significant relation to the relative viscosity of the local anaesthetic solution.

L3 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 2006161724 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16550876
TITLE: The use of a new viscoelastic substance combined with anaesthetic in cataract surgery by phacoemulsification.
AUTHOR: Bournas Panagiotis; Condilis Nicolas; Lioumi Dimitra; Kanellas Dimitrios; Syndikakis Konstantinos; Vaikoussis Emmanuel
CORPORATE SOURCE: Department of Ophthalmology, General State Hospital of Nikaia, Piraeus, Greece.
SOURCE: Annali italiani di chirurgia, (2005 Jul-Aug) Vol. 76, No. 4, pp. 383-8; discussion 388-9.
Journal code: 0372343. ISSN: 0003-469X.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (COMPARATIVE STUDY)
(EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(CLINICAL TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200604
ENTRY DATE: Entered STN: 23 Mar 2006
Last Updated on STN: 11 Apr 2006
Entered Medline: 10 Apr 2006

AB AIM OF THE STUDY: To compare and estimate the safety and efficacy of a new viscoelastic substance combined with anaesthetic used in phacoemulsification surgery. METHOD: Eight hundred seventy-four patients observed at the Department of Ophthalmology and the Department of Family Medicine of the General State Hospital of Nikea-Piraeus (Greece) submitted to a phacoemulsification surgery for cataract during a six-month period were randomly divided into two groups of 437 patients each. All patients were operated using the same scheme of anesthesia, consisting of ropivacaine drops 0.75% and lidocaine gel 2% immediately before surgery. Viscoelastic without anesthetic was used during the operation of the patients of group 1, while the new viscoelastic with anesthetic (sodium hyaluronate 1.5% and lidocaine 1%) (viscoanesthetic) was used in group 2. No intravenous sedation was given to either group. Patients were asked to complete a questionnaire including irritation or pain sensation during various phases of the operation, after the operation, as well as the degree of satisfaction from the anesthesia scheme. The participating surgeons were called to estimate post-operative corneal edema. RESULTS: In the first group of patients (viscoelastic without anesthetic) 15.6% of them reported pain during intraocular lens insertion, 24.6% reported burning sensation during acetylcholine injection, 17.4% reported pain during placement of the corneal suture, 4.1% immediate postoperative pain and 1.8% night pain. In the second group of patients (viscoelastic with anesthetic) the percentages were 1.8%, 3.2%, 4.3%, 3.6% and 1.4% respectively. 78.9% of the first group and 82.1% of the second group had no corneal edema on the first postoperative day. 91.1% of the patients of the first group and 97.3% of the second group were satisfied. CONCLUSION: The new combination of viscoelastic and anesthetic is a safe and efficient choice for the cataract surgeon who uses only anesthetic drops for cataract operations. It minimizes patients' complaints and helps in achieving better cooperation during cataract surgery.

L3 ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 88323622 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2458007
TITLE: Effects of macromolecular adjuvants on the duration of prilocaine. Experimental studies on the effect of variations of viscosity and sodium content and of inclusion of adrenaline.

AUTHOR: Renck H; Hassan H G; Lindberg B; Akerman B
CORPORATE SOURCE: Department of Anaesthesia, Malmo General Hospital, Sweden.
SOURCE: Acta anaesthesiologica Scandinavica, (1988 Jul) Vol. 32, No. 5, pp. 355-64.
Journal code: 0370270. ISSN: 0001-5172.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198810
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 29 Jan 1999
Entered Medline: 3 Oct 1988

AB Sodium hyaluronate (HA) and dextran (Dx) of different molecular weights and concentrations were used as adjuvants to prilocaine for studies of the duration of infraorbital nerve block in the rat (IONB) and spinal anaesthesia in the mouse (SA). A positive relation was found between duration of block on the one hand and the concentration as well as the molecular weight of the adjuvant on the other. A direct relation was found between the duration of block and the viscosity of the anaesthetic solution. Low-sodium-content solutions of plain prilocaine caused a markedly prolonged duration of the most profound degrees of IONB as compared to medium- or high-sodium-content solutions, while no differences between the solutions were found for the weakest intensity of IONB studied or for SA. Solutions of low-sodium-content containing prilocaine and HA were associated with significant prolongations of IONB and SA as compared to corresponding solutions of medium- or high-sodium content. Inclusion of adrenaline, 5 micrograms/ml, in solutions containing prilocaine and Dx significantly prolonged the duration of the most profound degrees of IONB and of SA. By contrast, the inclusion of adrenaline in solutions containing prilocaine and HA did not prolong the duration of IONB or SA. It is concluded that modulations of the viscosity of local anaesthetic solutions by the addition of macromolecular compounds strongly affect the duration of peripheral and central nerve blocks in experimental animals. A further prolongation is accomplished by reducing the sodium content of the solutions and, in the case of Dx-containing solutions, by inclusion of adrenaline in the anaesthetic solution. The possible mechanisms of these actions are discussed.

L3 ANSWER 3 OF 3 MEDLINE on STN
ACCESSION NUMBER: 85247331 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3874511
TITLE: Effects of adjuvants to local anaesthetics on their duration. III. Experimental studies of hyaluronic acid.
AUTHOR: Hassan H G; Akerman B; Renck H; Lindberg B; Lindquist B
SOURCE: Acta anaesthesiologica Scandinavica, (1985 May) Vol. 29, No. 4, pp. 384-8.
Journal code: 0370270. ISSN: 0001-5172.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198508
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varying degrees in a dose-dependent way by up to 500% of values obtained with plain prilocaine. The duration of degree 5 blocks produced by 0.5% etidocaine and 0.5% bupivacaine was also significantly prolonged when 0.4% HA was included to 206% and 282% of control, respectively, while blocks induced by 2% lidocaine were prolonged to 123% of control. The duration of motor block following spinal anaesthesia in the mouse was prolonged in a dose-dependent way when HA was added to prilocaine, bupivacaine and etidocaine. For solutions containing 0.4% HA, prolongations to 254%, 166% and 134% of control, respectively, were obtained. A concomitant increase of latency to onset of block and failure rate occurred with increasing concentrations of HA. The duration of corneal anaesthesia in the rabbit increased by 57% and 44% when 0.3% HA was added to prilocaine and bupivacaine, respectively. The duration of infiltration anaesthesia was not affected by the addition of HA to the local anaesthetic solutions. Addition of HA had no effect on the onset, depth and duration of prilocaine-induced block of the nervous transmission in vitro. The duration of infra-orbital nerve block and spinal anaesthesia shows a significant relation to the relative viscosity of the local anaesthetic solution.

L6 ANSWER 1 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2004622055 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15518947
TITLE: [Soft tissue filling with hyaluronic acid].
Les comblements par l'acide hyaluronique.
AUTHOR: Ascher B; Cerceau M; Baspeyras M; Rossi B
CORPORATE SOURCE: Clinique IENA, 11, rue Fresnel, 75116 Paris, France..
benjaminascher@wanadoo.fr
SOURCE: Annales de chirurgie plastique et esthetique, (2004 Oct)
Vol. 49, No. 5, pp. 465-85. Ref: 64
Journal code: 8305839. ISSN: 0294-1260.
PUB. COUNTRY: France
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20 Dec 2004
Last Updated on STN: 25 Jan 2005
Entered Medline: 24 Jan 2005

AB PHYSIOLOGY AND PHARMACOLOGY: Hyaluronan was discovered by Karl Meyer in 1934 in the vitreous humor of cattle eye. Hyaluronic acid, (AH), is a natural polysaccharide and a ubiquitous component of the extra cellular matrix. It is largely biocompatible and has a short half life. In the early 1990's, preceded by the use of bovine collagen, AH started to be employed in the fields of Dermatology and Plastic Surgery; currently it is a major intervention product in both soft tissue augmentation and facial volume loss treatments. Often well tolerated, AH, has high water retention properties and is an effective tissue volumizer. Industry first attempted to extract AH from rooster comb, then through bacterial fermentation and succeeded in increasing its lifespan by cross linking. However, industrially produced AH can contain residues from the manufacturing process. It thus appears critical to us to be informed of the process used in manufacturing AH including the reticulant utilized. Manufacturers should be legally required to publish this data as well as to conduct physiochemical follow-up studies over the short, mid and long terms. LEGAL CONSIDERATIONS: In Europe, CE marking is a prerequisite to market injectable products. However, a CE marking does not necessarily imply that the product's efficacy and side effects have been assessed objectively in clinical studies. However, this marking is expected to fall into line with the US legislation, where the marketing of any medicinal product is subject to FDA approval, based on comprehensive animal and clinical studies and on more systematic and better centralised side effect reporting. We have examined most of the products used in Europe and internationally in 2004, whether of animal or bacterial origin, reticulated or non-reticulated, and used to restore, increase volume or as a product vector. Before injecting these products, it is essential to have a thorough understanding of their absolute and relative contraindications and anaesthetic requirements, differences between types of wrinkles to fill in and indicated techniques, differences between concerned regions or tissues, and the impact of associated cosmetic treatments. These resorbable injectable products have mild and, more importantly, short-lived side effects. However, in patients with a relative contraindication, a double test is justified, as allergic reactions are known to occur in 1 to 3% of patients. It is also advisable not to inject HA in a site previously injected with a non-resorbable product. More precise statistics on results and side effects based on double-blind randomised studies are still wanting, due to the lack of legal requirement and effective centralisation of data. Therefore, all side effects must be reported to improve our knowledge as well as the safety of injections. CONCLUSION: Although their duration of effect is limited, HA products are the most commonly used fillers, before collagens.

Many questions have yet to be answered, but they produce very significant results in filling procedures. Both clinicians and patients praise these products for their tolerance, resorbable nature, and limited side effects.

L6 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2004405154 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15309218
TITLE: [Safety profile of 185 ultrasound-guided intra-articular injections for treatment of rheumatic diseases of the hip]. Profilo di sicurezza di 185 iniezioni intra-articolari sotto guida ecografica nelle coxopatie.
AUTHOR: Migliore A; Tormenta S; Martin Martin L S; Valente C; Massafra U; Latini A; Alimonti A
CORPORATE SOURCE: Dipartimento Medicina Interna, Ospedale S.Pietro-Fatebenefratelli, Rome, Italy.. alberto.migliore@tin.it
SOURCE: Reumatismo, (2004 Apr-Jun) Vol. 56, No. 2, pp. 104-9. Journal code: 0401302. ISSN: 0048-7449.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (COMPARATIVE STUDY)
(ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 14 Aug 2004
Last Updated on STN: 24 Sep 2004
Entered Medline: 23 Sep 2004

AB OBJECTIVE: We have developed a standardized technique for intra-articular injection of the hip joint with the purpose of extending routine intra-articular injection of hyaluronans and steroids to the hip, as commonly used in the knee. The purpose of this study was to examine the safety of this technique in an extended series of patients. METHODS: A 7 MHz linear or 3.5 MHz convex transducer was used with a sterilized biopsy guide attached. Intra-articular (IA) injection was performed by inserting into the biopsy guide a 20 gauge needle with the anterosuperior approach. Then, using biopsy real-time guidance software, the needle was advanced into the anterior capsular recess, at the level of the femoral head. RESULTS: The standardised technique was used to inject 97 patients (114 hips) with 185 injections of either steroid/local anaesthetic (10) or hyaluronan (175) over a three-year period. The treatment was well tolerated with few, and exclusively local, side effects. No systemic side effects or joint infections were observed in our study. The colour Doppler vision allowed us to avoid injecting blood vessels. In all cases direct visualization of needle introduction and progression into the articular space was shown by on-screen guidance. Ultrasound guidance is more economic and faster in comparison to the TC or fluoroscopic guidance. Contrary to TC or fluoroscopic techniques ultrasound does not require use of radiations or iodized contrast. CONCLUSION: Our data suggest that the administration of hyaluronans or steroids with ultrasound-guided intra-articular injection is a safe technique for treatment of rheumatic diseases of the hip.

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:333586 CAPLUS
DOCUMENT NUMBER: 140:344879
TITLE: Combination preparation of hyaluronic acid and at least one local anesthetic and use for the treatment of arthritis
INVENTOR(S): Wohlrab, David
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032943	A1	20040422	WO 2003-EP10822	20030930
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10246340	A1	20040429	DE 2002-10246340	20021004
AU 2003271660	A1	20040504	AU 2003-271660	20030930
EP 1545564	A1	20050629	EP 2003-753479	20030930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006122147	A1	20060608	US 2005-529924	20051128

PRIORITY APPLN. INFO.: DE 2002-10246340 A 20021004
WO 2003-EP10822 W 20030930

AB The invention relates to a combination preparation comprising an active substance A selected among the group that consists of hyaluronic acid and the salts and fragments thereof, at least one active substance B selected among the group of local anesthetics and the derivs. thereof, and other optional additives. Said combination prepns. are used for the medical treatment of degenerative and traumatic diseases of all joints, the treatment of articular cartilage damages and cartilage bone damages, lesions of a meniscus or an intervertebral disk such as arthrosis, articular rheumatism, osteochondrolysis, flake fractures, and meniscus lesions, and the treatment of skin modifications or mucosal modifications, also according to cosmetic aspects. Thus lidocaine hydrochloride and hyaluronic acid were added in powder form to RPMI solution and sterile filtered. The biocompatibility of the solution was tested on human chondrocytes that were isolated from knee joint cartilage; the influence of the combination solution on the proliferation of the chondrocytes is also reported.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 1999019994 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9803153
TITLE: The lubricating ability of biomembrane models with dipalmitoyl phosphatidylcholine and gamma-globulin.
AUTHOR: Higaki H; Murakami T; Nakanishi Y; Miura H; Mawatari T; Iwamoto Y
CORPORATE SOURCE: Department of Intelligent Machinery and Systems, Faculty of

Engineering, Kyushu University, Hakozaki Fukuoka, Japan.
SOURCE: Proceedings of the Institution of Mechanical Engineers. Part H, Journal of engineering in medicine, (1998) Vol. 212, No. 5, pp. 337-46.
Journal code: 8908934. ISSN: 0954-4119.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 3 Dec 1998

AB Two kinds of friction tests were conducted to investigate the lubricating effect of the injection of amphiphilies on the osteoarthritic joint. The effects of the addition of L alpha-dipalmitoyl phosphatidyl-choline (L alpha-DPPC) riposomes and gamma-globulin in a saline solution of sodium hyaluronate (HA) were evaluated through pendulum friction tests. The frictional characteristics of pig shoulder joints were confirmed to depend on the viscosity of the lubricants only in the physiologically low load condition and in the condition immediately after loading. Detergent (polyoxyethylene p-t-octylphenyl ether) was successfully used to remove adsorbed films from the articular surfaces. The friction coefficient of natural synovial joints was significantly increased in a mode of mixed lubrication with the HA solution of 0.2 g/dl by the treatment of the surface with the detergent. The addition of L alpha-DPPC riposomes or gamma-globulin significantly improved the boundary lubricating ability of the articular surfaces treated with the detergent, depending on the quantity of those additives. It appears that the L alpha-DPPC riposomes and gamma-globulin can form protective films on the articular surfaces like a biomembrane. Moreover, the reciprocating frictional behaviour in sliding pairs of pig articular cartilages and glass plates was studied in order to elucidate the tribological role of those constituents in the boundary lubricating film on the articular surface. Pig synovial fluid and water solutions of HA were used as lubricants. The synovial fluid had superior lubricating ability compared to the HA solution of equivalent viscosity under a physiologically high load condition. This fact seems to be responsible for the boundary lubricating ability of constituents other than hyaluronic acid. Langmuir-Blodgett (LB) films of L alpha-DPPC on the glass plate were kept at a low and stable friction coefficient, depending on the number of film layers. In conditions of mixed films with L alpha-DPPC and gamma-globulin, the frictional behaviour was improved by increasing the quantity of gamma-globulin. A model is proposed in which the effective adsorbed films are composed of proteins, phospholipids and other conjugated constituents on the articular surfaces to be accurate in describing the boundary lubricating mechanism. The mechanism is controlled by hydrophobic groups in those amphiphilies.

L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:562713 CAPLUS
DOCUMENT NUMBER: 136:228928
TITLE: Detection of superficial zone protein in human and animal body fluids by cross-species monoclonal antibodies specific to superficial zone protein
AUTHOR(S): Su, Jui-Lan; Schumacher, Barbara L.; Lindley, Kathie M.; Soloveychik, Vitaliy; Burkhart, William; Triantafillou, James A.; Kuettner, Klaus; Schmid, Thomas
CORPORATE SOURCE: Department of Protein Sciences, GlaxoSmithKline, Research Triangle Park, NC, USA
SOURCE: Hybridoma (2001), 20(3), 149-157
CODEN: HYBRDY; ISSN: 0272-457X
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this report we describe the purification of human superficial zone protein (SZP), the generation of cross-species monoclonal antibodies (MAbs) and the detection of this protein in human and animal body fluids. Human SZPs, used as immunizing antigens, were purified either from culture media of human cartilage organ cultures or from human synovial fluids. The immunizing antigens were mixed with RIBI adjuvant in one of three forms: nonmodified SZP, superficial zone protein-keyhole limpet hemocyanin conjugate (SZP-KLH), or a mixture of superficial zone protein and hyaluronic acid (SZP-HA). A panel of MAbs including GW4.23, S6.79, S13.52, S13.233, and S17.109 were generated and characterized. Monoclonal antibody (MAb) S6.79, an IgG2b with KD 3.14+10-9 M from SZP-KLH immunization, is of particular interest. It reacts strongly to a large mol. weight form of SZP in both ELISA and Western blotting. It stains the most superficial layer of articular cartilage in immunohistochem., whereas the middle and deep zones of cartilage are not stained. When MAb S6.79 was applied to Western blots of human body fluids, a strong 345-kDa band was detected in samples of synovial fluid and weaker bands of similar size were detected in samples of plasma and serum. MAb S6.79 also showed cross-species immunoreactivity with SZP in samples of synovial fluids harvested from bovine, dog, guinea pig, and rabbit, as demonstrated by Western blotting and antibody absorption expts. This cross-species MAb will be a useful tool in human and animal model studies for monitoring SZP levels and tissue distribution. It may help define the roles of SZP in normal articular joints and may be of diagnostic or prognostic value for the measurement of SZP in pathol. conditions such as osteoarthritis, rheumatoid arthritis, and camptodactyly-arthropathy-coxa vara-peri-carditis.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:3471 CAPLUS
DOCUMENT NUMBER: 124:105934
TITLE: Antiinflammatory effects of recombinant human Cu, Zn-superoxide dismutase (Cu, Zn-SOD; TSA-234)
AUTHOR(S): Saijo, Taketoshi; Fukuda, Shigeru; Ohta, Yoshikazu; Makino, Haruhiko
CORPORATE SOURCE: Drug Safety Research Laboratories, Takeda Chemical Industries, Ltd., Japan
SOURCE: Free Radicals in Clinical Medicine, Clinical Conference on Free Radicals, 9th, Kyoto, Feb. 11-12, 1993 (1994), Meeting Date 1993, 53-60. Editor(s): Kondo, Motoharu; Oyanagui, Yoshihiko; Yoshikawa, Toshikazu. Nihon-Igakukan: Bunkyo-ku, Japan.
CODEN: 62DTAQ

DOCUMENT TYPE: Conference
LANGUAGE: Japanese
AB Antiinflammatory effects of TSA-234 were studied in vivo and in vitro. TSA-234, given intra-articularly, showed a significant inhibitory effects on sodium urate-induced arthritis in dog knees and carrageenin-induced one in rabbit ones. The agent, at 1 mg/kg, i.v. significantly inhibited ischemic paw edema in mice. The agent, at the doses of 0.125 and 8 mg/kg, i.v. significantly inhibited carrageenin-induced paw edema in rats and reversed passive Arthus reaction in the rat skin, resp. The agent at the dose of 8 mg/kg, s.c. slightly inhibited both adjuvant arthritis and type II collagen-induced arthritis in rats. TSA-234 significantly inhibited damage of chondrocytes, reduction in viscosity of hyaluronic acid and osteoathrosis-derived joint fluid, inactivation of α1-protease inhibitor and delayed gelation of collagen which induced by active oxygen species (mainly O-2) generated in the system of hypoxanthine-xanthine oxidase. These results suggest that TSA-234 will be useful with an intra-articular injection on the therapy of osteoarthrosis in knees.

L8 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:81553 CAPLUS
DOCUMENT NUMBER: 122:556
TITLE: Anti-inflammatory effects of recombinant human Cu,Zn-superoxide dismutase (Cu,Zn-SOD:TSA-234)
AUTHOR(S): Saijo, T.; Fukuda, S.; Ohta, Y.; Makino, H.
CORPORATE SOURCE: Pharm. Dev. Div., Takeda Chem. Ind., Ltd., Takatsuki, Japan
SOURCE: International Congress Series (1994), 1058(Frontiers of Reactive Oxygen Species in Biology and Medicine), 389-92
CODEN: EXMDA4; ISSN: 0531-5131
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Anti-inflammatory effects of TSA-234 were studied in vivo and in vitro systems. In vivo systems, TSA-234 given intra-articularly at the dose of 0.25-1 mg/site showed a significant inhibitory effect on sodium urate-induced knee arthritis in dogs as well as carrageenin-induced one in rabbits. This compound, 1 mg/kg i.v., significantly inhibited ischemic paw edema in mice. The compound significantly inhibited carrageenin-induced paw edema in rats at the dose of 0.125 mg/kg i.v., and reversed passive Arthus reaction in the rat skin at the dose of 8 mg/kg i.v. TSA-234, 8 mg/kg s.c., slightly inhibited both adjuvant-and type II collagen-induced arthritis in rats. In vitro systems, TSA-234 (0.1-100 ug/mL) significantly inhibited damage of chondrocytes, reduction in viscosity of hyaluronic acid and osteoarthrosis-derived joint fluid, inactivation of α1-protease inhibitor and delayed gelation of collagen which were induced by the active oxygen species (mainly O2-) generated in the hypoxanthine-xanthine oxidase system. These results suggest that TSA-234 will be useful for the therapy of osteoarthrosis in the knee by an intra-articular administration.

L8 ANSWER 8 OF 11 MEDLINE on STN
ACCESSION NUMBER: 2005258193 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15899053
TITLE: Intra-articular injections of high-molecular-weight hyaluronic acid have biphasic effects on joint inflammation and destruction in rat antigen-induced arthritis.
AUTHOR: Roth Andreas; Mollenhauer Jurgen; Wagner Andreas; Fuhrmann Renee; Straub Albrecht; Venbrocks Rudolf A; Petrow Peter; Brauer Rolf; Schubert Harald; Ozegowski Jorg; Peschel Gundela; Muller Peter J; Kinne Raimund W
CORPORATE SOURCE: Department of Orthopaedics, Rudolf-Elle Hospital, Friedrich Schiller University Jena, Eisenberg, Germany.. ajroth@gmx.de

SOURCE: Arthritis research & therapy, (2005) Vol. 7, No. 3, pp. R677-86. Electronic Publication: 2005-03-31. Journal code: 101154438. E-ISSN: 1478-6362.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 19 May 2005 Last Updated on STN: 20 Jan 2006 Entered Medline: 19 Jan 2006

AB To assess the potential use of hyaluronic acid (HA) as adjuvant therapy in rheumatoid arthritis, the anti-inflammatory and chondroprotective effects of HA were analysed in experimental rat antigen-induced arthritis (AIA). Lewis rats with AIA were subjected to short-term (days 1 and 8, n = 10) or long-term (days 1, 8, 15 and 22, n = 10) intra-articular treatment with microbially manufactured, high-molecular-weight HA (molecular weight, 1.7 x 10(6) Da; 0.5 mg/dose). In both tests, 10 buffer-treated AIA rats served as arthritic controls and six healthy animals served as normal controls. Arthritis was monitored by weekly assessment of joint swelling and histological evaluation in the short-term test (day 8) and in the long-term test (day 29). Safranin O staining was employed to detect proteoglycan loss from the epiphyseal growth plate and the articular cartilage of the arthritic knee joint. Serum levels of IL-6, tumour necrosis factor alpha and glycosaminoglycans were measured by ELISA/kit systems (days 8 and 29). HA treatment did not significantly influence AIA in the short-term test (days 1 and 8) but did suppress early chronic AIA (day 15, $P < 0.05$); however, HA treatment tended to aggravate chronic AIA in the long-term test (day 29). HA completely prevented proteoglycan loss from the epiphyseal growth plate and articular cartilage on day 8, but induced proteoglycan loss from the epiphyseal growth plate on day 29. Similarly, HA inhibited the histological signs of acute inflammation and cartilage damage in the short-term test, but augmented acute and chronic inflammation as well as cartilage damage in the long-term test. Serum levels of IL-6, tumour necrosis factor alpha, and glycosaminoglycans were not influenced by HA. Local therapeutic effects of HA in AIA are clearly biphasic, with inhibition of inflammation and cartilage damage in the early chronic phase but with promotion of joint swelling, inflammation and cartilage damage in the late chronic phase.

L8 ANSWER 9 OF 11 MEDLINE on STN
ACCESSION NUMBER: 2003212169 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12723984
TITLE: Efficacy of treatment with glycosaminoglycans on experimental collagen-induced arthritis in rats.
AUTHOR: Campo Giuseppe M; Avenoso Angela; Campo Salvatore; Ferlazzo Alida M; Altavilla Domenica; Calatroni Alberto
CORPORATE SOURCE: Department of Biochemical, Physiological and Nutritional Sciences, School of Medicine, University of Messina, Messina, Italy.. gcampo@unime.it
SOURCE: Arthritis research & therapy, (2003) Vol. 5, No. 3, pp. R122-31. Electronic Publication: 2003-03-06. Journal code: 101154438. E-ISSN: 1478-6362.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 8 May 2003 Last Updated on STN: 19 Aug 2003 Entered Medline: 18 Aug 2003

AB To evaluate the antioxidant activity of the glycosaminoglycans hyaluronic acid (HYA) and chondroitin-4-sulphate (C4S), we used a rat model of collagen-induced arthritis (CIA). Arthritis was induced in Lewis rats by multiple intradermal injections of 250 microl of emulsion containing bovine type II collagen in complete Freund's adjuvant at the base of the tail and into three to five other sites on the back. Rats were challenged again with the same antigen preparation 7 days later. Disease developed about 11 days after the second immunization. The effects of treatment in the rats were monitored by biochemical parameters and by macroscopic and histological evaluations in blood, synovial tissue and articular cartilage. Arthritis produced the following symptoms: severe periarticular erythema, edema and inflammation in the hindpaws; membrane peroxidation in the cartilage of the joints; endogenous antioxidant wasting; high tumour necrosis factor-alpha (TNF-alpha) plasma levels; and synovial neutrophil accumulation. Treatment with HYA and C4S, starting at the onset of arthritis for 10 days, limited the erosive action of the disease in the articular joints of knee and paw, reduced lipid peroxidation, restored the endogenous antioxidants reduced glutathione (GSH) and superoxide dismutase, decreased plasma TNF-alpha levels, and limited synovial neutrophil infiltration. These data confirm that erosive destruction of the joint cartilage in CIA is due at least in part to free radicals released by activated neutrophils and produced by other biochemical pathways. The beneficial effects obtained with the treatment suggest that HYA and C4S could be considered natural endogenous macromolecules to limit erosive damage in CIA or as a useful tool with which to study the involvement of free radicals in rheumatoid arthritis.

L8 ANSWER 10 OF 11 MEDLINE on STN
ACCESSION NUMBER: 2003169884 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12688421
TITLE: Aromatic trap analysis of free radicals production in experimental collagen-induced arthritis in the rat: protective effect of glycosaminoglycans treatment.
AUTHOR: Campo Giuseppe M; Avenoso Angela; Campo Salvatore; Ferlazzo Alida; Altavilla Domenica; Micali Carmelo; Calatroni Alberto
CORPORATE SOURCE: Department of Biochemical, Physiological and Nutritional Sciences, School of Med., University of Messina, Policlinico Universitario, Torre Biologica, 5o piano, I-98125-Messina, Italy.. gcampo@unime.it
SOURCE: Free radical research, (2003 Mar) Vol. 37, No. 3, pp. 257-68.
Journal code: 9423872. ISSN: 1071-5762.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 16 Apr 2003
Last Updated on STN: 9 Sep 2003
Entered Medline: 8 Sep 2003

AB Many findings demonstrated that Glycosaminoglycans (GAGs) and Proteoglycans (PGs) possess antioxidant activity. Collagen-induced arthritis (CIA) is an experimental animal model similar to human rheumatoid arthritis (RA) in which free radicals are involved. Sodium salicylate can be used as a chemical trap for hydroxyl radicals (OH*), the most damaging reactive oxygen species (ROS), yielding 2,5-dihydroxybenzoic acid), (2,5-DHBA) and 2,3-dihydroxybenzoic acid (2,3-DHBA). The measurement of these two acids in the plasma allows to indirectly assess the production of OH* radicals. The aim of the study was to investigate the effect of hyaluronic acid (HYA) (30 mg/kg i.p.) or chondroitin-4-sulphate (C4S) (30 mg/kg i.p.), on free radical production

in Lewis rats subjected to CIA. After the immunization with bovine collagen type II in complete Freund's adjuvant, rats developed an erosive hind paw arthritis, that produced high plasma OH* levels assayed as 2,3-DHBA and 2,5-DHBA, primed lipid peroxidation, evaluated by analyzing conjugated dienes (CD) in the articular cartilage; decreased the concentration of endogenous vitamin E (VE) and catalase (CA) in the joint cartilage; enhanced macrophage inflammatory protein-2 (MIP-2) serum levels and increased elastase (ELA) evaluated as an index of activated leukocyte polymophonuclear (PMNs) accumulation in the articular joints. The administration of HYA and C4S starting at the onset of arthritis (day 11) for 20 days, limited inflammation and the clinical signs in the knee and paw, reduced OH* production, decreased CD levels, partially restored the endogenous antioxidants VE and CA, reduced MIP-2 serum levels and limited PMNs infiltration. The results indicate that the GAGs HYA and C4S significantly reduce free radical production in CIA and could be used as a tool to investigate the role of antioxidants in RA.

L8 ANSWER 11 OF 11 MEDLINE on STN
ACCESSION NUMBER: 2001411779 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11461663
TITLE: Detection of superficial zone protein in human and animal body fluids by cross-species monoclonal antibodies specific to superficial zone protein.
AUTHOR: Su J L; Schumacher B L; Lindley K M; Soloveychik V; Burkhart W; Triantafillou J A; Kuettner K; Schmid T
CORPORATE SOURCE: Department of Protein Sciences, GlaxoSmithKline, Research Triangle Park, NC 27709, USA.. JS2097@GSK.com
CONTRACT NUMBER: 2P50-AR39239 (NIAMS)
SOURCE: Hybridoma, (2001 Jun) Vol. 20, No. 3, pp. 149-57. Journal code: 8202424. ISSN: 0272-457X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 1 Oct 2001
Last Updated on STN: 1 Oct 2001
Entered Medline: 27 Sep 2001

AB In this report we describe the purification of human superficial zone protein (SZP), the generation of cross-species monoclonal antibodies (MAbs) and the detection of this protein in human and animal body fluids. Human SZPs, used as immunizing antigens, were purified either from culture media of human cartilage organ cultures or from human synovial fluids. The immunizing antigens were mixed with RIBI adjuvant in one of three forms: nonmodified SZP, superficial zone protein-keyhole limpet hemocyanin conjugate (SZP-KLH), or a mixture of superficial zone protein and hyaluronic acid (SZP-HA). A panel of MAbs including GW4.23, S6.79, S13.52, S13.233, and S17.109 were generated and characterized. Monoclonal antibody (MAb) S6.79, an IgG2b with K(D) 3.14 x 10(-9) M from SZP-KLH immunization, is of particular interest. It reacts strongly to a large molecular weight form of SZP in both enzyme-linked immunosorbent assay (ELISA) and Western blotting. It stains the most superficial layer of articular cartilage in immunohistochemistry, whereas the middle and deep zones of cartilage are not stained. When MAb S6.79 was applied to Western blots of human body fluids, a strong 345-kDa band was detected in samples of synovial fluid and weaker bands of similar size were detected in samples of plasma and serum. MAb S6.79 also showed cross-species immunoreactivity with SZP in samples of synovial fluids harvested from bovine, dog, guinea pig, and rabbit, as demonstrated by Western blotting and antibody absorption experiments. This cross-species MAb will be a useful tool in human and animal model studies for monitoring SZP levels and tissue distribution.

It may help define the roles of SZP in normal articular joints and may be of diagnostic or prognostic value for the measurement of SZP in pathological conditions such as osteoarthritis, rheumatoid arthritis, and camptodactyly-arthropathy-coxa vara-pericarditis.

L8 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:424002 CAPLUS
DOCUMENT NUMBER: 142:475677
TITLE: Intra-articular injections of high-molecular-weight hyaluronic acid have biphasic effects on joint inflammation and destruction in rat antigen-induced arthritis
AUTHOR(S): Roth, Andreas; Mollenhauer, Juergen; Wagner, Andreas; Fuhrmann, Renee; Straub, Albrecht; Venbrocks, Rudolf A.; Petrow, Peter; Braeuer, Rolf; Schubert, Harald; Ozegowski, Joerg; Peschel, Gundela; Mueller, Peter J.; Kinne, Raimund W.
CORPORATE SOURCE: Department of Orthopaedics, 'Rudolf-Elle' Hospital, Friedrich Schiller University Jena, Eisenberg, Germany
SOURCE: Arthritis Research & Therapy (2005), 7(3), R677-R686
CODEN: ARTRCV; ISSN: 1478-6362
URL: http://arthritis-research.com/content/pdf/ar1725.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB To assess the potential use of hyaluronic acid (HA) as adjuvant therapy in rheumatoid arthritis, the anti-inflammatory and chondroprotective effects of HA were analyzed in exptl. rat antigen-induced arthritis (AIA). Lewis rats with AIA were subjected to short-term (days 1 and 8, n = 10) or long-term (days 1, 8, 15 and 22, n = 10) intra-articular treatment with microbially manufactured, high-mol.-weight HA (mol. weight, 1.7 + 106 Da; 0.5 mg/dose). In both tests, 10 buffer-treated AIA rats served as arthritic controls and six healthy animals served as normal controls. Arthritis was monitored by weekly assessment of joint swelling and histol. evaluation in the short-term test (day 8) and in the long-term test (day 29). Safranin O staining was employed to detect proteoglycan loss from the epiphyseal growth plate and the articular cartilage of the arthritic knee joint. Serum levels of IL-6, tumor necrosis factor alpha and glycosaminoglycans were measured by ELISA/kit systems (days 8 and 29). HA treatment did not significantly influence AIA in the short-term test (days 1 and 8) but did suppress early chronic AIA (day 15, $P < 0.05$); however, HA treatment tended to aggravate chronic AIA in the long-term test (day 29). HA completely prevented proteoglycan loss from the epiphyseal growth plate and articular cartilage on day 8, but induced proteoglycan loss from the epiphyseal growth plate on day 29. Similarly, HA inhibited the histol. signs of acute inflammation and cartilage damage in the short-term test, but augmented acute and chronic inflammation as well as cartilage damage in the long-term test. Serum levels of IL-6, tumor necrosis factor alpha, and glycosaminoglycans were not influenced by HA. Local therapeutic effects of HA in AIA are clearly biphasic, with inhibition of inflammation and cartilage damage in the early chronic phase but with promotion of joint swelling, inflammation and cartilage damage in the late chronic phase.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:333401 CAPLUS
DOCUMENT NUMBER: 139:301585
TITLE: Efficacy of treatment with glycosaminoglycans on experimental collagen-induced arthritis in rats
AUTHOR(S): Campo, Giuseppe M.; Avenoso, Angela; Campo, Salvatore; Ferlazzo, Alida M.; Altavilla, Domenica; Calatroni, Alberto
CORPORATE SOURCE: Department of Biochemical, Physiological and Nutritional Sciences, University of Messina, Messina,

Italy
SOURCE: Arthritis Research & Therapy (2003), 5(3), R122-R131
CODEN: ARTRCV; ISSN: 1478-6362
URL: http://arthritis-research.com/content/pdf/ar748.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB To evaluate the antioxidant activity of the glycosaminoglycans hyaluronic acid (HYA) and chondroitin-4-sulfate (C4S), we used a rat model of collagen-induced arthritis (CIA). Arthritis was induced in Lewis rats by multiple intradermal injections of 250 μl of emulsion containing bovine type II collagen in complete Freund's adjuvant at the base of the tail and into three to five other sites on the back. Rats were challenged again with the same antigen preparation 7 days later. Disease developed about 11 days after the second immunization. The effects of treatment in the rats were monitored by biochem. parameters and by macroscopic and histol. evaluations in blood, synovial tissue and articular cartilage. Arthritis produced the following symptoms: severe periarticular erythema, edema and inflammation in the hindpaws; membrane peroxidn. in the cartilage of the joints; endogenous antioxidant wasting; high tumor necrosis factor-α (TNF-α) plasma levels; and synovial neutrophil accumulation. Treatment with HYA and C4S, starting at the onset of arthritis for 10 days, limited the erosive action of the disease in the articular joints of knee and paw, reduced lipid peroxidn., restored the endogenous antioxidants reduced glutathione (GSH) and superoxide dismutase, decreased plasma TNF-α levels, and limited synovial neutrophil infiltration. These data confirm that erosive destruction of the joint cartilage in CIA is due at least in part to free radicals released by activated neutrophils and produced by other biochem. pathways. The beneficial effects obtained with the treatment suggest that HYA and C4S could be considered natural endogenous macromols. to limit erosive damage in CIA or as a useful tool with which to study the involvement of free radicals in rheumatoid arthritis.
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:116245 CAPLUS
DOCUMENT NUMBER: 139:51062
TITLE: Aromatic trap analysis of free radicals production in experimental collagen-induced arthritis in the rat: Protective effect of glycosaminoglycans treatment
AUTHOR(S): Campo, Giuseppe M.; Avenoso, Angela; Campo, Salvatore; Ferlazzo, Alida; Altavilla, Domenica; Micali, Carmelo; Calatroni, Alberto
CORPORATE SOURCE: Department of Biochemical, Physiological and Nutritional Sciences, School of Med., Policlinico Universitario, Torre Biologica, University of Messina, Messina, I-98125, Italy
SOURCE: Free Radical Research (2003), 37(3), 257-268
CODEN: FRARER; ISSN: 1071-5762
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many findings demonstrated that glycosaminoglycans (GAGs) and proteoglycans (PGs) possess antioxidant activity. Collagen-induced arthritis (CIA) is an exptl. animal model similar to human rheumatoid arthritis (RA) in which free radicals are involved. Sodium salicylate can be used as a chemical trap for hydroxyl radicals (OH•), the most damaging reactive oxygen species (ROS), yielding 2,5-dihydroxybenzoic acid, (2,5-DHBA) and 2,3-dihydroxybenzoic acid (2,3-DHBA). The measurement of these two acids in the plasma allows to indirectly assess the production of

OH• radicals. The aim of the study was to investigate the effect of hyaluronic acid (HYA) (30 mg/kg i.p.) or chondroitin-4-sulfate (C4S) (30 mg/kg i.p.), on free radical production in Lewis rats subjected to CIA. After the immunization with bovine collagen type II in complete Freund's adjuvant, rats developed an erosive hind paw arthritis, that produced high plasma OH• levels assayed as 2,3-DHBA and 2,5-DHBA, primed lipid peroxidn., evaluated by analyzing conjugated dienes (CD) in the articular cartilage; decreased the concentration of endogenous vitamin E (VE) and catalase (CA) in the joint cartilage; enhanced macrophage inflammatory protein-2 (MIP-2) serum levels and increased elastase (ELA) evaluated as an index of activated leukocyte polymophonuclear (PMNs) accumulation in the articular joints. The administration of HYA and C4S starting at the onset of arthritis (day 11) for 20 days, limited inflammation and the clin. signs in the knee and paw, reduced OH• production, decreased CD levels, partially restored the endogenous antioxidants VE and CA, reduced MIP-2 serum levels and limited PMNs infiltration. The results indicate that the GAGs HYA and C4S significantly reduce free radical production in CIA and could be used as a tool to investigate the role of antioxidants in RA.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:47269 CAPLUS
DOCUMENT NUMBER: 138:112495
TITLE: Gel compositions of carboxymethyl cellulose-cocrosslinked hyaluronic acid and medical materials containing the compositions
INVENTOR(S): Yamamoto, Osamu; Umeda, Toshihiko
PATENT ASSIGNEE(S): Denki Kagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003019194	A	20030121	JP 2001-210493	20010711

PRIORITY APPLN. INFO.: JP 2001-210493 20010711

AB The gel compns. are manufactured by freezing aqueous solns. with pH ≤3.5 containing hyaluronic acid (I) and CM-cellulose (II) and thawing the frozen product, and show dissoln. rates of I and II ≤50% each in neutral solution at 25° after a day or at 37° after 12 h. Also claimed are medical materials, e.g. tissue adhesion-preventing materials, artificial articular cartilage, ophthalmic adjuvants, wound dressings, artificial skin, artificial synovial fluid, artificial extracellular matrix, etc., containing the gel compns. The gel compns. are noncytotoxic and have good biocompatibility and longer in vivo retention time. Na hyaluronate (2 + 105 Da) and Aqualon 7H3SXF-PH (CM-cellulose Na, etherification degree 0.9) were dissolved in H2O at concns. of both substances 0.5% each. The solution was adjusted to pH 1.5 with HCl, frozen in a Petri dish for 5 days, soaked in a phosphate-buffered saline at 5° for 24 h, washed with water, and dried to give a gel sheet. Usefulness of the sheet to prevent postoperative adhesion was shown in rat uterine horn model.

L10 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:151006 CAPLUS
DOCUMENT NUMBER: 146:308815
TITLE: Intra-articular injection of a nutritive mixture solution protects articular cartilage from osteoarthritic progression induced by anterior cruciate ligament transection in mature rabbits: a randomized controlled trial
AUTHOR(S): Park, Yoo-Sin; Lim, Si-Woong; Lee, Il-Hoon; Lee, Tai-Jin; Kim, Jong-Sung; Han, Jin So
CORPORATE SOURCE: Institute of Biomedical Science, College of Medicine 1F, Hanyang University, Seoul, 133-791, S. Korea
SOURCE: Arthritis Research & Therapy (2007), 9(1), No pp. given
CODEN: ARTRCV; ISSN: 1478-6362
URL: http://arthritis-research.com/content/pdf/ar2114.pdf
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Osteoarthritis (OA) is a degenerative disease which disrupts collagenous matrix of articular cartilage, and is difficult to cure because articular cartilage is a nonvascular tissue. Treatment of OA has targeted macromol. substitutes for cartilage components, such as hyaluronic acid or genetically engineered materials. However, the goal of this study is to examine whether intra-articular injection of the elementary nutrients restores the matrix of arthritic knee joints of mature animals. A nutritive mixture solution (NMS) was composed to elementary nutrients such as glucose or dextrose, amino acids and ascorbic acid. It was administered five times, at the 6th, 8th, 10th, 13th, and 16th weeks, into the unilateral anterior cruciate ligament transected (ACLT) knee joints of mature New Zealand White rabbits. It was compared to normal saline (NS)-injection effect. OA progression was histopathol. evaluated by hematoxylin and eosin (H and E) staining, by the Mankin grading method, and by SEM at the 19th week. NMS-injection decreased progressive erosion of articular cartilage overall compared to NS-injection ($p < 0.01$), and showed no differences compared to normal cartilage which did not undergo ACLT, by Mankin grading method. H&E staining and SEM results also showed that NMS-injection, as apposed to NS-injection, restored the cartilage matrix that is known to be composed of a collagen and proteoglycan (PG) network. Thus, NMS-injection is a potent treatment that significantly retards OA progression, which in turn prevents progressive destruction of joints and functional loss in mature animals.
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:569718 CAPLUS
DOCUMENT NUMBER: 105:169718
TITLE: Articular chondrocytes cultured in agarose gel for study of chondrocytic chondrolysis
AUTHOR(S): Aydelotte, Margaret B.; Schleyerbach, Rudolf; Zeck, Bill J.; Kuettner, Klaus E.
CORPORATE SOURCE: Rush-Presbyterian-St. Luke's Med. Cent., Rush Med. Coll., Chicago, IL, 60612, USA
SOURCE: Articular Cartilage Biochem., Workshop Conf. Hoechst-Werk Albert (1986), Meeting Date 1985, 235-56. Editor(s): Kuettner, Klaus E.; Schleyerbach, Rudolf; Hascall, Vincent C. Raven: New York, N. Y.
CODEN: 55FCAT
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Proteoglycan metabolism was studied in chondrocytes from bovine articular cartilage cultured in suspension in a middle layer of a 1% agarose gel. The half-life (t1/2) of proteoglycans from cultures prelabeled with [35S]sulfate was taken as an indicator of chondrocytic chondrolysis. Retinol (5 μM) stimulated proteoglycan degradation as indicated by shortening their t1/2 (days) from 14.2 to 5.3, an action requiring protein formation, as seen by its blockage by cycloheximide. Proteoglycans extracted from the cell layer of both control and retinol-treated cultures declined in their ability to aggregate with exogenous hyaluronic acid with time in culture, indicating that the proteoglycans that diffuse into the medium represent degradation products of the extracellular matrix. Proteoglycan turnover was also stimulated by L-ascorbate both with and without retinol in the medium. A protease inhibitor-rich extract of bovine nasal septum cartilage (anti-invasion factor) retarded the retinol-induced degradation of proteoglycans. Chondrocytes cultured in agarose are useful for the study of the effects of potentially therapeutic agents on the time course of native digestion and its degradation products.

L10 ANSWER 3 OF 3 MEDLINE on STN
ACCESSION NUMBER: 2007188988 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17257416
TITLE: Intra-articular injection of a nutritive mixture solution protects articular cartilage from osteoarthritic progression induced by anterior cruciate ligament transection in mature rabbits: a randomized controlled trial.
AUTHOR: Park Yoo-Sin; Lim Si-Woong; Lee Il-Hoon; Lee Tae-Jin; Kim Jong-Sung; Han Jin Soo
CORPORATE SOURCE: Institute of Biomedical Science, College of Medicine 1F, Hanyang University, Haengdang-dong 17, Seongdong-gu, Seoul, 133-791, South Korea.. hidocys@hanyang.ac.kr
SOURCE: Arthritis research & therapy, (2007) Vol. 9, No. 1, pp. R8. Journal code: 101154438. E-ISSN: 1478-6362.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200704
ENTRY DATE: Entered STN: 30 Mar 2007
Last Updated on STN: 1 May 2007
Entered Medline: 30 Apr 2007

AB Osteoarthritis (OA) is a degenerative disease that disrupts the collagenous matrix of articular cartilage and is difficult to cure because articular cartilage is a nonvascular tissue. Treatment of OA has targeted macromolecular substitutes for cartilage components, such as hyaluronic acid or genetically engineered materials. However, the goal of the present study was to examine whether intra-articular injection of the elementary nutrients restores the matrix of arthritic knee joints in mature animals. A nutritive mixture solution (NMS) was composed of elementary nutrients such as glucose or dextrose, amino acids and ascorbic acid. It was administered five times (at weeks 6, 8, 10, 13 and 16) into the unilateral anterior cruciate ligament transected knee joints of mature New Zealand White rabbits, and the effect of NMS injection was compared with that of normal saline. OA progression was histopathologically evaluated by haematoxylin and eosin staining, by the Mankin grading method and by scanning electron microscopy at week 19. NMS injection decreased progressive erosion of articular cartilage overall compared with injection of normal saline ($P < 0.01$), and nms joints exhibited no differences relative to normal cartilage that had not undergone transection of the anterior cruciate ligament, as assessed using the mankin grading method. Haematoxylin and eosin staining and scanning

electron microscopy findings also indicated that nms injection, in contrast to normal saline injection, restored the cartilage matrix, which is known to be composed of a collagen and proteoglycan network. thus, nms injection is a potent treatment that significantly retards oa progression, which in turn prevents progressive destruction of joints and functional loss in mature animals.

L13 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:813780 CAPLUS
DOCUMENT NUMBER: 147:150218
TITLE: Cosmetic packs for skin whitening comprising increased amount of Phellinus linteus powder and its extract as active ingredients
INVENTOR(S): Choe, Ok Rye
PATENT ASSIGNEE(S): S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2007017566	A	20070212	KR 2007-6833	20070123

PRIORITY APPLN. INFO.: KR 2007-6833 20070123
AB A cosmetic pack composition comprising Phellinus linteus powder and its extract as active ingredients is provided to maximize skin-whitening effects of Phellinus linteus by increasing amount of Phellinus linteus component, and improve functionality of the composition by adding further nutrients useful for the skin. The cosmetic pack composition comprises 40-50 weight% of Phellinus linteus powder having 300-340 mesh, 2-3 weight% of honey, 3-5 weight% of glycerin, 5-7 weight% of propylene glycol, 1.5-2.5 weight% of collagen, 2-3 weight% of bees wax, 0.2-0.3 weight% of tocopherol, 1.8-2.5 weight% of squalene, 0.2-0.3 weight% of ascorbic acid, 1-3 weight% of hyaluronic acid, 1.5-2.5 weight% of polysorbate, and 25-30 weight% of the extract of Phellinus linteus, wherein the Phellinus linteus extract is prepared by heating the Phellinus linteus powder of 300-340 mesh in water at 100° for 8-10 h.

L13 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1175982 CAPLUS
DOCUMENT NUMBER: 145:495026
TITLE: Cosmetic formulations containing (2-hydroxyethyl)urea and a combination of active substances
PATENT ASSIGNEE(S): Beiersdorf A.-G., Germany
SOURCE: Ger. Gebrauchsmusterschrift, 30pp.
CODEN: GGXXFR
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 202006011472	U1	20061109	DE 2006-202006011472	20060724

PRIORITY APPLN. INFO.: DE 2006-202006011472 20060724
AB The invention concerns cosmetic compns. that contain: (a) (2-hydroxyethyl)urea; (b) urea; (c) one or more compds. selected from the group of: folic acid, D-biotin, coenzyme Q10, α-glucosylrutin, carnitine, natural and/or synthetic isoflavonoids, genistein, flavonoids, carotenes, creatines, creatinine, taurine, ascorbic acid and derivs., tocopherol and its ester, dihydroxyacetone; 8-hexadecene-1,16-dicarboxylic acid, glucosyl glyceride; hyaluronic acid with a medium mol. weight of 5 to 3000 Kilo-Dalton and/or licochalcone A. Other substances, e.g. sunscreens can be added. Thus an O/W lotion contained(weight/weight): glycerin 6; cetyl

palmitate 10.00; liquid paraffin 8.00; cetyl alc. 3.00; cyclomethicone 3.00; sorbitan stearate 2.00; aluminum starch octenyl succinate 1.50; phenoxyethanol 0.80; methylparaben 0.30; carbomer 0.25; propylparaben 0.10; sodium hydroxide 0.03; (2-hydroxyethyl)urea 6.00; urea 2.00; carnitine 3.00; water to 100.00.

L13 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:761929 CAPLUS
DOCUMENT NUMBER: 133:325490
TITLE: Capsule-containing cosmetic gel compositions
INVENTOR(S): Iwamoto, Atsuhiro
PATENT ASSIGNEE(S): Noevir Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000302662	A	20001031	JP 1999-113017	19990421
JP 3622832	B2	20050223		

PRIORITY APPLN. INFO.: JP 1999-113017 19990421

AB The invention relates to a cosmetic gel composition containing easily disintegrating capsules without causing skin irritation, wherein the capsules consist of agar and alginic acid polyvalent metal salt, and include cosmetic ingredients, and the capsules are dispersed in an aqueous gel containing NaOH and a C3-6 diol. Disintegrating capsules were prepared from calcium alginate 1, agar 1.5, water 95.5, dl-α- tocopherol 1, vitamin A palmitate 1 %. The capsules were dispersed in an aqueous gel containing carboxyvinyl polymer 42, sodium polyacrylate 2.1, 1,3-butanediol 30, ethanol 3.5, Me paraben 0.1, fragrance 0.02, 1 % hyaluronic acid solution 1, 1 % L-ascorbic acid solution 1.2, and water q.s. to 100 %.

L13 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:430648 CAPLUS
DOCUMENT NUMBER: 129:140491
TITLE: Dentifrice compositions containing hyaluronic acid and antioxidants for prevention and treatment of periodontal diseases
INVENTOR(S): Okata, Toshiyuki; Morishima, Seiji; Yoshikawa, Masaru
PATENT ASSIGNEE(S): Lion Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10182390	A	19980707	JP 1996-356313	19961225

PRIORITY APPLN. INFO.: JP 1996-356313 19961225

AB Title compns., which control active O formation, contain hyaluronic acid or its nontoxic salts and antioxidants. A mixture of K hyaluronate and ascorbyl palmitate at 0.5 and 3.0%, resp., in vitro showed 93.0% inhibition of phorbol myristate acetate-induced active O formation by rat peripheral blood polymorphonuclear leukocyte. A toothpaste was prepared from Al(OH)3 45.0, SiO2 2.0, sorbitol 25.0, Na CM-cellulose 1.0, sucrose monopalmitate 1.0, Na lauryl sulfate 1.5, Na saccharin 0.2, EtOH 0.1, Na benzoate 0.1, Na hyaluronate 0.1, Me salicylate 0.2, α-DL- tocopherol 1.0,

and H2O to 100.0 weight%.

L13 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:341137 CAPLUS
DOCUMENT NUMBER: 122:114972
TITLE: Phospholipid carriers with high capacity for lipophilic substances
INVENTOR(S): Hager, Joerg-Christian; Bentheimer, Wolfgang; Brock, Evelyn; Schmidt, Ursula
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer GmbH, Germany
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4322158	A1	19950112	DE 1993-4322158	19930703
DE 4322158	C2	19970410		
WO 9501776	A1	19950119	WO 1994-DE732	19940620

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: DE 1993-4322158 A 19930703
AB Title carriers comprise a mixture of liposomes and spherical or spheroidal lipid vesicles, where the vesicles contain ≥1 phospholipid and ≥1 lipophilic substance, in an aqueous or aqueous/organic medium. The mass ratio of liposome phospholipids to lipid vesicles is (5:1)-(1:5). The vesicles are evidently stabilized by an outer layer of phospholipids. The carrier shows a high capacity for both lipophilic substances, stored mainly in the vesicles, and hydrophilic substances, stored in the liposomes, and shows excellent uptake by the skin. Thus, 333.3 g of a 60 weight% solution of mixed phospholipids in propylene glycol was mixed with a solution of ascorbyl palmitate 0.5 in propylene glycol 26.7 g. Retinol palmitate 25 and tocopherol acetate 100 g were dissolved in 210.5 g of the above solution at 40°, and this solution (150 g) was added to a solution of dexpanthenol 5.0, allantoin 2.0, hyaluronic acid 0.01, and trometamol 0.25 g in 507.0 g water with stirring to form a gel; the pH was adjusted to 6.7 with an aqueous solution containing 0.25 g trometamol. Application of this gel to the skin of patients with psoriasis or neurodermatitis (0.2 g/10 cm2 3 times a day for 14 days) resulted in 92 and 90% healing, resp.

L13 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:101963 CAPLUS
DOCUMENT NUMBER: 122:181194
TITLE: Fatty acid composition and functional properties of low density lipoprotein and oxidized LDL from human plasma
AUTHOR(S): Choi, Jae-Hoon; Cho, Hyun-Mi; Son, Heung-Soo; Kim, Tae-Woong
CORPORATE SOURCE: Dept. of Biochemistry, Kangwon National University, Chuncheon, 200-701, S. Korea
SOURCE: Han'guk Yongyang Siklyong Hakhoechi (1994), 23(3), 402-8
CODEN: HYSHDL; ISSN: 0253-3154
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The fatty acid compns. of low-d. lipoprotein (LDL) from Koreans was compared with that of Westerners. The percentage of unsatd. fatty acids in Korean and Westerner LDL was .apprx.30% and 70%, resp., which means that the lipid oxidation of LDL in Westerners is more labile than that in

Koreans. Normal LDL was incubated with CuSO4 in PBS to induce peroxidn. of LDL, and it was tested by the detection of TBARS and free radicals. Then, ascorbate, α- tocopherol and hyaluronic acid were found to have antioxidants effects on LDL oxidation The amount of free radical increased as the extent of oxidation increased. The time course of free radical formation was similar to TBARS. Therefore, determination of free radicals by luminometer was much more convenient than that of TBARS.

L13 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:192577 CAPLUS
DOCUMENT NUMBER: 108:192577
TITLE: Application of liposomes to cosmetics
AUTHOR(S): Suzuki, Kazushige; Sakon, Kenichi
CORPORATE SOURCE: Res. Dev. Dep., Noevir Co., Ltd., Yokaichi, 527, Japan
SOURCE: Fragrance Journal (1987), 15(6), 60-7
CODEN: FUJAD7; ISSN: 0288-9803
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 41 refs. on the preparation and utility of liposomes in cosmetics. Procedures of trapping of biol. active compds., such as placenta, α- tocopherol acetate, L-ascorbyl magnesium phosphate and bovine serum extract, into small or large unilamellar and multilamellar vesicles made of natural or hydrogenated lecithins are shortly described. Purity of lipids is of importance for making stable liposomes. Several prepns. containing collagen, elastin, hyaluronic acid, placenta, oryzanol, superoxide dismutase, vitamin E, etc., are mentioned.

L13 ANSWER 8 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2007076094 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17256782
TITLE: Primary graft nonfunction and Kupffer cell activation after liver transplantation from non-heart-beating donors in pigs.
AUTHOR: Monbaliu Diethard; van Pelt Jos; De Vos Rita; Greenwood Joanne; Parkkinen Jaakko; Crabbe Tina; Zeegers Marcel; Vekemans Katrien; Pincemail Joel; Defraigne Jean-Olivier; Fevery Johan; Pirenne Jacques
CORPORATE SOURCE: Department of Abdominal Transplant Surgery, University Hospitals Leuven, Leuven, Belgium.. Diethard.Monbaliu@uz.kuleuven.ac.be
SOURCE: Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society, (2007 Feb) Vol. 13, No. 2, pp. 239-47.
Journal code: 100909185. ISSN: 1527-6465.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200704
ENTRY DATE: Entered STN: 6 Feb 2007
Last Updated on STN: 13 Apr 2007
Entered Medline: 12 Apr 2007
AB More extensive use of non-heart-beating donors (NHBD) could reduce mortality on liver transplantation waiting lists, but this is associated with more primary nonfunction (PNF). We assessed which parameters are involved in the development of PNF in livers from NHBD in a previously validated pig liver transplantation model, in which livers were transplanted after exposure to incremental periods of warm ischemia. The risk of PNF was unacceptably high (>50%) when livers were exposed to >30 minutes' warm ischemia before a short cold ischemic period. This study

examined how PNF is affected by Kupffer cell activation (beta-galactosidase), the generation of cytokines tumor necrosis factor alpha and interleukin 6, antioxidant mechanisms (ascorbic acid, alpha-tocopherol, reduced glutathione), circulating redox-active iron, and sinusoidal endothelial cell function (hyaluronic acid clearance). Kupffer cells were more activated in PNF recipients, as suggested by higher beta-galactosidase levels (15 minutes after reperfusion), and secondarily, by higher production of tumor necrosis factor alpha and interleukin 6 (180 minutes after reperfusion). In addition, alpha-tocopherol and reduced glutathione were lower, and ascorbic acid and redox-active iron higher in PNF recipients. Finally, PNF grafts displayed progressively decreasing hyaluronic acid clearance (suggesting sinusoidal endothelial cell dysfunction) and parenchymal edema. Consequently, a reduced-flow phenomenon was documented. In grafts from NHBD that are destined to fail, beta-galactosidase activity (a surrogate of Kupffer cell activation) is higher, proinflammatory cytokines are overproduced, some antioxidant mechanisms fail, and circulating redox-active iron is more rapidly released. A no-flow phenomenon is eventually observed in these failing grafts.

L14 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:456852 CAPLUS
DOCUMENT NUMBER: 133:94510
TITLE: Skin protection agents containing a fragment mixture produced from hyaluronic acid by hydrolysis
INVENTOR(S): Wohlrab, Wolfgang; Neubert, Reinhard; Huschka, Christoph; Mueller, Peter-Juergen; Ozegowski, Joerg-Herman; Koegst, Dieter; Fries, Gerhard
PATENT ASSIGNEE(S): Esparma G.m.b.H., Germany; Hans-Knoell-Institut fuer Naturstoff-Forschung e.V.; Friedrich-Schiller-Universitaet Jena; Institut fuer Angewandte Dermatopharmazie an der MLU Universitaet Hautklinik
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038647	A1	20000706	WO 1999-EP10336	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1140006	A1	20011010	EP 1999-965544	19991222
EP 1140006	B1	20030723		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002533376	T	20021008	JP 2000-590601	19991222
AT 245410	T	20030815	AT 1999-965544	19991222
ES 2203238	T3	20040401	ES 1999-965544	19991222
US 6689349	B1	20040210	US 2001-868955	20010910

PRIORITY APPLN. INFO.: DE 1998-19860544 A 19981223
WO 1999-EP10336 W 19991222

AB An agent for the treatment and prophylaxis of functional and structural disorders of the skin caused by external factors contains hyaluronic acid which has been partially digested to terminally unsatd. fragments with a microbial hyaluronate lyase. Owing to the terminal double bonds, the fragments are active as antioxidants, radical scavengers, inflammation inhibitors, and inhibitors of photochem. reactions. The hyaluronic acid fragment mixture is processed into different galenic formulations to which other hydrophilic and/or lipophilic active ingredients and/or auxiliary substances can be added. The mixture is suitable for use in human and veterinary medicine in the treatment and/or prophylaxis of skin damage caused by environmental factors, including UV, as well as of dry skin and skin aging. Thus, biotechnol. produced hyaluronic acid (mean mol. weight 1800 kDa) was incubated with hyaluronate lyase from Streptococcus agalactiae to produce fragments with mean mol. weight 150 kDa. A hydrogel was prepared containing 2-ethylhexyl 4-methoxycinnamate 3.50, 1-(4-tert-butyl)-3-(4'-methoxyphenyl)propane-1,3-dione 1.00, tocopherol acetate 1.00, hyaluronic acid fragments 2.00, Carboset 514 (acrylate copolymer) 10.00, and EtOH to 100.00%.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:121100 CAPLUS
DOCUMENT NUMBER: 110:121100
TITLE: Skin cosmetics containing evening primrose oil and radical scavengers and spleen extracts
INVENTOR(S): Marty, Jean Pierre
PATENT ASSIGNEE(S): Roussel-UCLAF, Fr.
SOURCE: Fr. Demande, 8 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2606279	A1	19880513	FR 1986-16154	19861120
FR 2606279	B1	19940218		
PRIORITY APPLN. INFO.:			FR 1986-16154	19861120

AB Cosmetic and dermatol. compns. contain evening primrose oil, spleen tissue exts., and ≥1 radical scavengers and singlet O inhibitors . Radical scavengers are e.g. terpenes, lipid-soluble carrot exts., and α- tocopherol. These cosmetics retard the signs of aging of the skin. Evening primrose oil contains essential fatty acids that inhibit dryness of the skin, loss of elasticity, and transdermal loss of water. The formulations may optionally contain adenosine phosphate, e.g. ATP, and addnl. caffeine or theophylline that inhibits phosphodiesterase and cAMP degradation A cosmetic cream contained glucate SS 3, glucamate SSE-20 2, evening primrose oil 10, fatty acid esters 7, plant sterols 5, lipid-soluble carrot extract 0.2, α- tocopherol 0.05, UV absorbers 3, Mg Al silicate 1.2, spleen extract 5, preservatives q.s., Na pyrrolidonecarboxylate 2, hyaluronic acid 0.03, phosphorylated ATP riboside 0.025, cAMP 0.02, perfume 0.3, and H2O to 100% by weight

L14 ANSWER 3 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2003327383 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12856480
TITLE: Hypothalamic digoxin-mediated model for Parkinson's disease.
AUTHOR: Kurup Ravi Kumar; Kurup Parameswara Achutha
CORPORATE SOURCE: Department of Neurology, Medical College Hospital, Trivandrum, Kerala, India.. kvgnair@satyam.net.in
SOURCE: The International journal of neuroscience, (2003 Apr) Vol. 113, No. 4, pp. 515-36.
Journal code: 0270707. ISSN: 0020-7454.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 15 Jul 2003
Last Updated on STN: 30 Aug 2003
Entered Medline: 29 Aug 2003

AB The isoprenoid pathway produces four key metabolites important in cellular function--digoxin (endogenous membrane Na(+)-K+ ATPase inhibitor), dolichol (important in N-glycosylation of proteins), ubiquinone (free-radical scavenger), and cholesterol (component of cellular membranes). This study assessed the changes in the isoprenoid pathway and the consequences of its dysfunction in Parkinson's disease (PD). There was an elevation in plasma HMG CoA reductase activity, serum digoxin and dolichol levels, and a reduction in serum magnesium, RBC membrane Na(+)-K+

ATPase activity, and serum ubiquinone levels. Serum tryptophan, serotonin, strychnine, nicotine, and quinolinic acid were elevated, while tyrosine, morphine, dopamine, and noradrenaline were decreased. The total serum glycosaminoglycans (GAG) and glycosaminoglycan fractions (except chondroitin sulphates and hyaluronic acid), the activity of GAG degrading enzymes, carbohydrate residues of serum glycoproteins, the activity of glycohydrolase-beta galactosidase, and serum glycolipids were elevated. HDL cholesterol was reduced and free fatty acids increased. The RBC membrane glycosaminoglycans, hexose and fucose residues of glycoproteins and cholesterol were reduced, while phospholipid was increased. The activity of all serum free-radical scavenging enzymes, concentration of glutathione, alpha tocopherol , iron binding capacity, and ceruloplasmin decreased significantly in PD, while the concentration of serum lipid peroxidation products and nitric oxide increased. A dysfunctional isoprenoid pathway and related cascade are important in the pathogenesis of Parkinson's disease. A hypothalamic digoxin mediated model for Parkinson's disease is also postulated.

L14 ANSWER 4 OF 4 MEDLINE on STN
ACCESSION NUMBER: 1999248364 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10231507
TITLE: Impaired proliferation and increased L-lactate production of dermal fibroblasts in the GK-rat, a spontaneous model of non-insulin dependent diabetes mellitus.
AUTHOR: Hehenberger K; Hansson A; Heilborn J D; Abdel-Halim S M; Ostensson C G; Brismar K
CORPORATE SOURCE: Department of Molecular Medicine, The Endocrine and Diabetes Unit, Karolinska Institute, Stockholm, Sweden.. karin.hehenberger@molmed.ki.se
SOURCE: Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society, (1999 Jan-Feb) Vol. 7, No. 1, pp. 65-71. Journal code: 9310939. ISSN: 1067-1927.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 1 Jun 1999
Last Updated on STN: 1 Jun 1999
Entered Medline: 20 May 1999

AB Intact fibroblast function is required for normal wound healing. Although healing is generally accepted to be disturbed in non-insulin dependent diabetes mellitus, the signals modulating this disturbance are not fully understood. Therefore, we studied dermal fibroblasts from the GK rat, a non-insulin dependent diabetes mellitus model, and the Wistar rat (control) regarding growth characteristics, and L-lactate production at 5.5 mM and 25.5 mM glucose in the absence or presence of protein kinase C-inhibition, or alpha-tocopherol acetate. In addition, growth and L-lactate responses to hyaluronic acid were assessed under normal glucose conditions. At 5.5 mM glucose, the fibroblasts from the GK rat showed a lower proliferation rate during the first 24 hours, measured as DNA content, as compared to Wistar rats, i.e. at 8 hours GK was 57% of control, $p < 0.01$, at 24 hours GK was 60% of control, $p < 0.01$. The GK rat fibroblasts accumulated higher L-lactate levels in the media at 24-96 hours. Addition of glucose at a concentration of 25.5 mM decreased the total DNA content in GK rat fibroblast cultures to 74% ($p < 0.05$) and in control to 87% ($p < 0.05$), and increased L-lactate levels, measured at 48 hours. A protein kinase C-inhibitor, bisindolylmaleimide IX, increased DNA content and decreased L-lactate in both cell types during culture in high glucose, but only affected GK rat fibroblasts during normal glucose. Hyaluronic acid, increased DNA content in both types of

fibroblasts, GK: 139% ($p < 0.05$), control: 127% ($p < 0.05$) and reduced L-lactate production. The above observations indicate that GK rat fibroblast proliferation is suppressed when the cells are cultured in high glucose containing media. In addition, protein kinase C and hyaluronic acid might play a role as modulators of fibroblast proliferation during the diabetic state.

L15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:140410 CAPLUS
DOCUMENT NUMBER: 126:216657
TITLE: Wound therapeutic mixture containing medical grade hyaluronic acid and tissue culture grade plasma fibronectin in a delivery system that creates a moist environment which simulates in utero healing
INVENTOR(S): Taylor-McCord, Darlene
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5604200	A	19970218	US 1994-236176	19940502
PRIORITY APPLN. INFO.:			US 1994-236176	19940502

AB A wound therapeutic mixture is formulated to work alone or in combination with human growth factors, and is useful for treatment of burns, open sores, incisions, and wounds. The mixture is comprised of a medical grade hyaluronic acid (hyaluronan) and tissue culture grade plasma fibronectin in combination with calcium, phosphate, uric acid, urea, sodium, potassium, chloride, and magnesium, all elements found in amniotic fluid. The therapeutic mixture can be sterile or contain an FDA acceptable preservative system. The compns. may be in the form of a liquid, cream, ointment, gel, hydrogel, hydrocolloid or dressing. A therapeutic skin lotion contained water 73.44, Aloe vera gel 2.5, walnut oil 2, tocopherol acetate 2, glycerin 2, stearic acid 2, 1-hexadecanol 2, Polysorbate-60 2, apricot kernel oil 2, jojoba oil 2, glyceryl stearate 2, PEG-100 stearate 1, dimethicone 1, PVP 1, hyaluronic acid 0.5, fibronectin 0.5, Na 0.5, allantoin 0.5, triethanolamine 0.5, Carbomer-940 0.2, Cl 0.2, K 0.05, urea 0.06, Ca 0.05, phosphate 0.03, and Mg 0.01%.